REMARKS

In view of the foregoing claim amendments, and the remarks that follow, applicants respectfully submit that all of the pending claims are in condition for allowance.

Rejection of Claims 1, 67, 75, 82-88, and 91-97 Under 35 U.S.C. § 112, First Paragraph, As Failing to Comply With the Written Description Requirement

Applicants note that Claims 1 and 67 have been amended to recite that the (-)-camphene synthase encoded by the claimed nucleic acid molecules and vectors comprises an amino terminal half and a carboxy terminal half, wherein the carboxy terminal half comprises amino acid sequence motif DDXXD. Support for these claim amendments is found in the specification at least at page 64, lines 31-32.

Applicants submit that the claimed nucleic acid molecules are adequately described by: (1) the ability of the claimed nucleic acid molecules to hybridize under defined, stringent, hybridization conditions to a probe nucleic acid molecule; (2) the protein encoded by the nucleic acid molecule possesses (-)-camphene synthase activity; and (3) the presence of the characteristic sequence motif DDXXD within the carboxy terminal half of the encoded protein. Applicants note that an assay for identifying (-)-camphene synthase activity is described in the specification in Example 3.

Applicants respectfully request withdrawal of the rejection of Claims 1, 67, 75, 82-88, and 91-97 under 35 U.S.C. § 112, first paragraph (written description).

Rejection of Claims 1, 67, 75, 82-88, and 91-97 Under 35 U.S.C. § 112, First Paragraph, for Lack of Enablement

The Examiner argues that the full scope of the claimed invention is not enabled because the specification does not provide sufficient guidance with respect to where and how to obtain isolated nucleic acid molecules that encode a (-)-camphene synthase, and that hybridize to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours, followed by one wash in

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

0.5 X SSC at 55°C for 30 minutes. In particular, the Examiner argues that one cannot predictably obtain nucleic acid molecules that encode a (-)-camphene synthase from any unspecified source, as monoterpene synthases such as (-)-camphene synthase enzymes appear to be unique to certain members of the plant kingdom.

Applicants submit that one of ordinary skill in the art can readily identify plant species that produce (-)-camphene, and which therefore produce a (-)-camphene synthase that catalyzes the formation of the (-)-camphene. For example, included herewith, as Attachment A, is a photocopy of page 261 of the Merck Index (11th edition, 1989, Merck & Co., Inc., Rahway, New Jersey) that discloses, under entry number 1736 (Camphene) that (-)-camphene (also referred to as *l*-camphene) occurs in many essential oils, such as in turpentine (the generic name for the essential oils of conifers), in bergamot oil, in oil of citronella, neroli, ginger, and valerian. Additionally, included herewith as Attachment B, is a photocopy of page 66 of the Essential Oils, Volume II (E. Guenther ed., R.E. Krieger, New York, N.Y., 1975) which discloses that "*d*-, *l*- and *dl*-Camphene occur in nature quite widely distributed", and that *l*-Camphene is found "in Siberian pine needle oil, in the oil distilled from the needles of *Abies concolor*, of *Pinus palustris*, in American and Russian turpentine oil, in Ceylon citronella oil, valerian oil, etc."

Applicants submit that the plants that produce (-)-camphene must, therefore, produce a (-)-camphene synthase that catalyzes the formation of the (-)-camphene. Consequently, applicants submit that the prior art provides one of ordinary skill in the art with ample guidance to identify plant species from which to isolate a nucleic acid molecule encoding (-)-camphene synthase.

Additionally, applicants submit that the present specification provides ample guidance for isolating a nucleic acid molecule (*e.g.*, cDNA molecule) encoding a (-)-camphene synthase from a plant source. For example, the present application describes, in Example 12, probes and hybridization conditions that can be used to screen nucleic acid libraries to identify nucleic acid molecules that encode monoterpene synthases, including (-)-camphene synthases. Example 3 of

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

the present application describes an assay that can be used to determine the principal product produced by a candidate monoterpene synthase protein that utilizes geranyl diphosphate as a substrate. As set forth at page 10, lines 1-5, of the present application, a (-)-camphene synthase principally produces (-)-camphene from geranyl diphosphate.

Again by way of example, pages 20-22 of the present application disclose representative eukaryotic expression systems for expressing nucleic acid molecules that encode (-)-camphene synthase. Page 22, line 9, through page 24, line 29, describes representative methods for stably transforming a plant with a nucleic acid molecule that encodes a monoterpene synthase, such as (-)-camphene synthase, for expression of the protein therein. Again, by way of example, page 26, line 19, through page 28, line 6, discloses representative methods for expressing monoterpene synthase proteins in prokaryotes. Thus, applicants submit that the prior art, together with the teachings of the present application, amply describe sources of (-)-camphene synthases, and methods for their cloning and expression.

The examiner further argues that the effect of expressing a nucleic acid encoding a (-)-camphene synthase in any unspecified eukaryotic cell is unpredictable, since monoterpenes such as camphene that would be produced as a consequence of (-)-camphene synthase expression are known to be toxic to certain types of eukaryotic cells. Applicants submit that the prior art, and the teachings of the present specification, provide ample guidance for expressing a nucleic acid molecule encoding a (-)-camphene synthase in any eukaryotic cell. Assuming, as the examiner suggests, that some eukaryotic cells may react adversely to the expression of camphene therein, applicants submit that undue experimentation is not required to identify eukaryotic cell types that tolerate expression of (-)-camphene. In this regard, submitted herewith as Attachment C is the declaration of inventor Rodney B Croteau (hereinafter referred to as the Croteau Declaration). The Croteau Declaration describes the successful expression of a (-)-camphene synthase cDNA, and production of (-)-camphene, in eukaryotic *Saccharomyces cerevisiae* cells.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

In view of the foregoing arguments, and the evidence presented in the Croteau Declaration, applicants respectfully request withdrawal of the rejection of Claims 1, 67, 75, 82-88, and 91-97 under 35 U.S.C. § 112, first paragraph (enablement).

CONCLUSION

In view of the foregoing claim amendments, arguments, and the evidence presented in the Croteau Declaration, applicants respectfully submit that all of the pending claims are in condition for allowance. Reconsideration and favorable action are requested.Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS[PLLC]

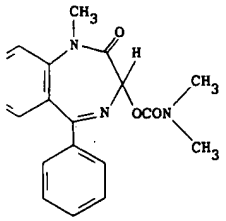
Barry F. McGurl
Registration No. 43,340
Direct Dial No. 206.695.1775

I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first class mail with postage thereon fully prepaid and addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the below date.

Date: January 6, 2005

BFM:ejh/tmm

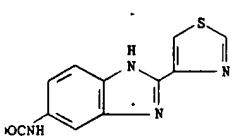
LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100



owder from ethyl acetate, mp 173
noderately sol in water. LD_{50} orally
00 mg/kg (Ferrini).
trolled substance (depressant) listed in
eral Regulations, Title 21 Part 1308.12

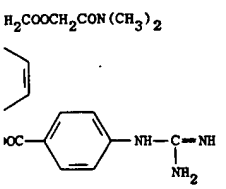
lytic.

ole. *[2-(4-Thiazolyl)-1H-benzimida*
d 1-methylethyl ester; 2-(4-thiazolyl)
nate isopropyl ester; 5-isopropoxyca
zolyl)benzimidazole; 5-isopropoxyca
zole; isopropyl 2-(4-thiazolyl)-5-benz
MK-905; Bonlam; Bovicam; Cambe
n; Novazole; Noviben. $C_{14}H_{14}N_4O_2S$;
61%, H 4.67%, N 18.53%, O 10.58%,
activity studies: Hoff, Fisher, S. Afr.
) to Merck & Co.), *C.A.* **72,** 90461n
perientia **26,** 550 (1970). Clinical studies
and swine: Egerton *et al., Res. Vet. Sci.*
70).



ystalline solid, mp 238-240° (dec). Sol
lformamide; sparingly sol in acetone
e; very slightly sol in 0.1*M* HCl. Pract
ane and water (0.02 mg/ml). Stable in
ge of pH 1 to 12. uv max (0.1*N* HCl)
40, 670).
Anthelmintic.

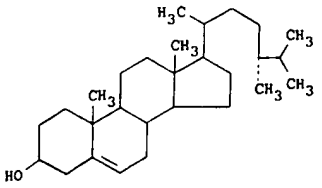
4-[[4-[(Aminoiminomethyl)amino]be
ic acid 2-(dimethylamino)-2-oxoeth
carbamoylmethyl-*p*-(*p*-guanidinoben
ate. $C_{20}H_{22}N_4O_5$; mol wt 398.43.
N 14.06%, O 20.08%. Orally active
ytic enzyme inhibitor with anti-trypsi
tivities, related structurally to gabexate
ii *et al.*, **Ger. pat. 2,548,886** corresp to
(1976, 1977 both to Ono). Enzym
. Tamura *et al., Biochim. Biophys. Acta*
hibition of exptl tumors in mice: *Ibid.*
959 (1981), *C.A.* **96,** 97304v (1982); *Ibid.* **73,** 108 (1982), *C.A.* **96,** 155
of acute exptl pancreatitis: S. Takasu
6 (1982). Absorption and excretion
uhin Kenkyu **13,** 756 (1982), *C.A.*



onate, $C_{21}H_{26}N_4O_8S$, *Foy-305, cam*

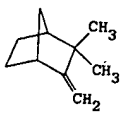
mesylate, Foypan. Solid from methanol/ether, mp 150-155°. Sol in water.
THERAP CAT: Enzyme inhibitor (proteinase).

1735. Campesterol. *(24R)-Ergost-5-en-3β-ol.* $C_{28}H_{48}O$; mol wt 400.66. C 83.93%, H 12.08%, O 3.99%. Small amounts are found in rape-seed oil derived from *Brassica campestris* L., *Cruciferae,* in soybean oil, and in wheat germ oil. Isoln: Fernholz, MacPhillamy, *J. Am. Chem. Soc.* **63,** 1155 (1941). Structure: Fernholz, Ruigh, *ibid.* 1157. Synthesis: Tarzia *et al., Gazz. Chim. Ital.* **97,** 102 (1967), *C.A.* **67,** 32883q (1967).



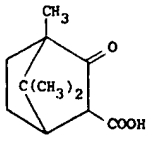
Crystals from acetone, mp 157-158°. $[\alpha]_D^{23}$ −33° (22.5 mg in 5 ml chloroform).
Acetate, $C_{30}H_{50}O_2$, crystals from alc, mp 137-138°. $[\alpha]_D^{23}$ −35° (28.8 mg in 1 ml chloroform).

1736. Camphene. *2,2-Dimethyl-3-methylenebicyclo-[2.2.1]heptane; 2,2-dimethyl-3-methylenenorbornane;* 3,3-dimethyl-2-methylenenorcamphane. $C_{10}H_{16}$; mol wt 136.23. C 88.16%, H 11.84%. Occurs in many essential oils, such as turpentine (*levo* and *dextro* forms), in cypress oil (*dextro* form), in camphor oil from species of *Lauraceae (dextro*), in bergamot oil, in oil of citronella, neroli, ginger, valerian. Reviews on isolation, preparation and properties: J. L. Simonsen, *The Terpenes* **vol. II** (Cambridge Univ. Press, 1949) pp 280-322; E. Guenther, *The Essential Oils* **vol. II** (Van Nostrand, 1949) pp 66-70. Synthesis: G. W. Hana, H. Koch, *Ber.* **111,** 2527 (1968).



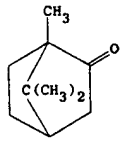
dl-Form, cubic crystals from alcohol. Large dodecahedra by slow sublimation. Volatilizes on exposure to air. Insipid odor. mp 51-52°. bp_{760} 158.5-159.5°; bp_{100} 92.4°; bp_{16} 55-56°. d_4^{54} 0.8422. n_D^{54} 1.45514. Practically insol in water. Moderately sol in alcohol; sol in ether, cyclohexane, cyclohexene, dioxane, chloroform.
d-Form, mp 52°. $[\alpha]_D^{17}$ +103.5° (c = 9.67 in ether). d_4^{50} 0.8486. n_D^{50} 1.4605.
l-Form, mp 52°. $[\alpha]_D^{21}$ −119.11° (c = 2.33 in benzene). d_4^{54} 0.8422. n_D^{60} 1.4620.

1737. *d*-Camphocarboxylic Acid. *4,7,7-Trimethyl-3-oxobicyclo[2.2.1]heptane-2-carboxylic acid; d-2-oxo-3-bornanecarboxylic acid; d*-3-camphorcarboxylic acid; *d*-2-oxo-3-camphanecarboxylic acid; *d*-3-carboxy-2-bornanone; *d*-3-carboxy-2-camphanone. $C_{11}H_{16}O_3$; mol wt 196.24. C 67.32%, H 8.22%, O 24.46%. Prepd by carboxylation of *d*-camphor: Brühl, *Ber.* **24,** 3373 (1891).



Crystals from benzene, water, ether, or 50% alcohol. mp 127-128°. Sparingly sol in cold water, more sol in warm water; sol in alcohol, ether, chloroform, in about 2 parts boiling benzene. Sparingly sol in cold benzene. Practically insol in cold petr ether; very slightly sol in boiling petr ether. For soln contg 0.38 g in 25 ml solvent: $[\alpha]_D$ +18° (benzene), +60° (alcohol), +73.3° (water).
Ammonium salt, $C_{11}H_{19}NO_3$, *camphydryl, Canfoxil, camphor solubilized.*
Basic bismuth salt, $C_{33}H_{46}Bi_2O_{11}$, *Bismo-Cymol, Angimuth, Camphobismol.* Prepn: Raiziss, Clemence, U.S. pat. **1,921,638** (1933 to Abbott). Powder. Odor of camphor. Practically insoluble in water; soluble in methanol, ether, benzene, oils.
THERAP CAT: Basic bismuth salt formerly as antisyphilitic.

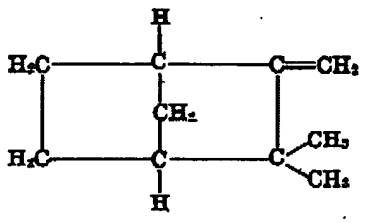
1738. Camphor. *1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one;* 2-bornanone; 2-camphanone; 2-keto-1,7,7-trimethylnorcamphane; gum camphor; Japan camphor; Formosa camphor; laurel camphor. $C_{10}H_{16}O$; mol wt 152.23. C 78.89%, H 10.60%, O 10.51%. Occurs in all parts of the camphor tree, *Cinnamomum camphora* T. Nees & Ebermeier, *Lauraceae. Habit:* Java, Sumatra, China (central provinces), Japan, Formosa, Brazil. Obtained by steam distillation from comminuted trees which should be at least 50 years old. Description of various indigenous processes: Gubelmann, Elley, *Ind. Eng. Chem.* **26,** 589 (1934); G. Etzel in Kirk-Othmer *Encyclopedia of Chemical Technology,* **vol. 4** (Wiley, New York, 2nd ed., 1964) pp 54-58. Modern processes start with vinyl chloride and cyclopentadiene to obtain the important intermediate dehydronorbornyl chloride. Review of syntheses: K. Alder in *New Methods of Preparative Organic Chemistry* (New York, 1948); A. F. Thomas in *The Total Synthesis of Natural Products* **vol. 2,** J. ApSimon, Ed. (Wiley-Interscience, New York,1973) pp 149-154. More than three-fourths of the camphor sold in the U.S. is produced synthetically (usually from pinene), and most is sold in the racemic form, although the U.S.P. specifies the *d*-form. Configuration: Freudenberg *et al., Ann.* **594,** 76 (1955). Toxicity: A. Smith, G. Margolis, *Am. J. Pathol.* **30,** 857 (1954).



Translucent mass with crystalline fracture. Rhombohedral crystals from alcohol. Cubic crystals by melting and chilling. Familiar fragrant and penetrating odor. Slightly bitter and cooling taste. d_4^{25} 0.992. mp 179.75° (corr., open capillary, 2 mm diam). bp 204°. Sublimes appreciably at room temp and press. *Keep in tight containers away from heat.* At 80° and 12 mm press 14% sublimes within 60 minutes. Very volatile in steam. $[\alpha]_D^{25}$ +41° to +43° (c = 10 in U.S.P. alcohol) according to U.S.P. specif. The water content of the ethanol influences the rotation considerably. $[\alpha]_D^{20}$ +43.8° (c = 7.5 in abs alcohol). uv max ($CHCl_3$): 292 nm. At 25° one gram dissolves in about 800 ml water (giving a colloidal soln), in 1 ml alcohol, 1 ml ether, 0.5 ml chloroform, 0.4 ml benzene, 0.4 ml acetone, 1.5 ml oil of turpentine, 0.5 ml glacial acetic acid. Sol in aniline, nitrobenzene, carbon disulfide, tetralin, decalin, methylhexalin, petr ether, in the higher alcohols, in fixed and volatile oils. Also sol in concd mineral acids in phenol, in liquid NH_3 and in liquid SO_2. Camphor has a peculiar tenacity and cannot be powdered in a mortar unless it is moistened with an organic solvent. Liquefies when triturated with chloral hydrate, menthol, resorcinol, salol, β-naphthol, thymol, phenol, urethan. LD_{50} i.p. in mice: 3000 mg/kg (Smith, Margolis).
Incompat: Incompatible with potassium permanaganate; salts of any kind should not be added to camphor water.
Human Toxicity: Ingestion or injection may cause nausea, vomiting, vertigo, mental confusion, delirium, clonic convulsions, coma, respiratory failure, death, *Clinical Toxicology of Commercial Products,* R. E. Gosselin *et al.,* Eds. (Williams & Wilkins, Baltimore, 4th ed., 1976) Section III, pp 77-79.
USE: Excellent plasticizer for cellulose esters and ethers; used in manuf of plastics, esp celluloid; in lacquers and varnishes; in explosives; in pyrotechnics; as moth repellent; in embalming fluids; in manuf cymene; as preservative in phar-

Camphene

$C_{10}H_{16}$ Mol. Weight 136.23



Camphene is the only $C_{10}H_{16}$ crystalline hydrocarbon found so far in essential oils. Due to its crystalline nature it has been obtained in pure form and free from isomers, which cannot be claimed of other hydrocarbons. However, in only a few cases has it been possible to isolate camphene from essential oils in crystalline form—for example, from Siberian pine needle oil.

Camphene is a bicyclic terpene of considerable interest and capable of many reactions as it tends to undergo intramolecular rearrangements. Camphene, therefore, has been the subject of numerous investigations, the discussion of which would lead too far in these pages. Suffice it to mention only that camphene can be prepared synthetically by the elimination of hydrogen chloride from bornyl chloride, or from isobornyl chloride, or even more conveniently by dehydration of isoborneol with zinc chloride. However, in this case a mixture of several hydrocarbons will be obtained.

Occurrence.—*d*-, *l*- and *dl*-Camphene occur in nature quite widely distributed:

d-Camphene has been identified in Siberian pine needle oil, in oil of cypress, camphor, lemon, orange, spike lavender, *Eucalyptus globulus*, nutmeg, ginger, etc.

l-Camphene is also found in Siberian pine needle oil, in the oil distilled from the needles of *Abies concolor*, of *Pinus palustris*, in American and Russian turpentine oil, in Ceylon citronella oil, valerian oil, etc.

dl-Camphene, too, has been found in numerous volatile oils.

Isolation.—As pointed out, the isolation of camphene from essential oils by mere crystallization has been possible only in a few instances. In most cases it will be necessary to resort to fractional distillation, or to employ an indirect method of isolation from the corresponding camphene fraction of an essential oil by converting the hydrocarbon into its chloride (with the theoretical amount of hydrogen chloride in ethereal solution), and by regenerating the camphene with alkali (see "Identification").

Identification.—Camphene may be identified by several methods.

(1) If the essential oil contains sufficient quantities of camphene, this terpene may be separated in crystalline form, the crystals melting at 51°–52°. It is, however, always advisable to confirm the identity of camphene by hydrating it to isoborneol m. 212°, whereby some borneol is also formed. The isoborneol can be further characterized by the preparation of its bromal compound m. 71°–72°, its phenylurethane m. 138°–139°, and its *p*-nitrob their identification.)

For the hydration of camp the following procedure:

Heat 100 parts of the cam of glacial acetic acid and 1(mixture will first separate in a slightly reddish color. A acetate, wash it repeatedly solution of 50 g. of potassiu add water. The isoborneol v tion from petroleum ether. (about 212°) must be undert would sublime.

When following Bertram that, in addition to isoborn isoborneol prepared by thi ylurethanes of both borneol tives should be used for thei

(2) Meerwein and van Em tity (but no excess) of hydro phene forms true camphene 125°–127°. The true camph and is extremely unstable: it

If camphene is further tre hydrochloric acid, the result somewhat impure form.

Camphene can be regenera chloride by the action of al chloride are optically active had been prepared. This met only if the corresponding fra

(3) If only small quantities tion may be difficult. The be potassium permanganate sol be characterized through its

(4) Lipp,[4] and Hückel et a acterize this hydrocarbon. I *l*- as m. 84°–85°, $[\alpha]_D$ −146° studies on an optically homo with these properties (after +153° 24′ (in benzene), $[\alpha]_D^{2}$ alcohol) m. 85°–86° gave rot (in alcohol).

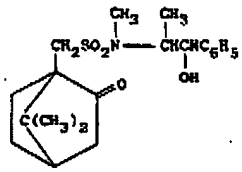
Properties.—Camphene faint camphoraceous odor influence of air and light t

As camphene may be ol ties by solution in alcoho should lend itself to isolati

Crystals from acetone. mp 157-158°. $[\alpha]_D^{25}$ −33° (22.5 mg in 5 ml chloroform).

Acetate, $C_{20}H_{29}O_2$, crystals from alc, mp 137-138°. $[\alpha]_D^{25}$ −35° (28.8 mg in 1 ml chloroform).

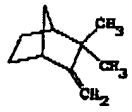
1707. Camphamedrine. *N-(β-Hydroxy-α-methylphenethyl)-N-methyl-10-camphorsulfonamide; N*-camphosulfonylephedrine; *d*-1-phenyl-2-(*N*-methyl-*β*-camphosulonylamino)propanol; Camphotone; Cardenyl. $C_{20}H_{29}NO_4S$; mol wt 379.52. C 63.30%, H 7.70%, N 3.69% O 16.86%, S 8.45%. Prepd from *β*-camphosulfonyl chloride and ephedrine: Ledrut, U.S. pat. 2,640,076 (1953 to Luxema).



Crystals, mp 157-160°. Sol in chloroform, acetone, benzene; slightly sol in cold water. uv max: 252, 258, 264.5 nm.

THERAP CAT: Analeptic.

1708. Camphene. *2,2-Dimethyl-3-methylenebicyclo-[2.2.1]heptane; 2,2-dimethyl-3-methylenenorbornane;* 3,3-dimethyl-2-methylenenorcamphane. $C_{10}H_{16}$; mol wt 136.23. C 88.16%, H 11.84%. Occurs in many essential oils, such as turpentine (*levo* and *dextro* forms), in cypress oil (*dextro* form), in camphor oil from species of *Lauraceae (dextro)*, in bergamot oil, in oil of citronella, neroli, ginger, valerian. Reviews on isolation, preparation and properties: J. L. Simonsen, *The Terpenes* vol. II (Cambridge Univ. Press, 1949) pp 280-322; E. Guenther, *The Essential Oils* vol. II (Van Nostrand, 1949) pp 66-70. Synthesis: G. W. Hana, H. Koch, *Ber.* 111, 2527 (1968).

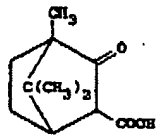


dl-Form, cubic crystals from alcohol. Large dodecahedra by slow sublimation. Volatilizes on exposure to air. Insipid odor. mp 51-52°. bp_{760} 158.5-159.5°; bp_{200} 92.4°; bp_{14} 55-56°. d_4^{54} 0.8422. n_D^{55} 1.45514. Practically insol in water. Moderately sol in alcohol; sol in ether, cyclohexane, cyclohexene, dioxane, chloroform.

d-Form, mp 52°. $[\alpha]_D^{27}$ +103.5° (c = 9.67 in ether). d_4^{50} 0.8486. n_D^{50} 1.4605.

l-Form, mp 52°. $[\alpha]_D^{21}$ −119.11° (c = 2.33 in benzene). d_4^{54} 0.8422. n_D^{55} 1.4620.

1709. *d*-Camphocarboxylic Acid. *4,7,7-Trimethyl-3-oxobicyclo[2.2.1]heptane-2-carboxylic acid; d-2-oxo-3-bornanecarboxylic acid; d*-3-camphorcarboxylic acid; *d*-2-oxo-3-camphanecarboxylic acid; *d*-3-carboxy-2-bornanone; *d*-3-carboxy-2-camphanone. $C_{11}H_{16}O_3$; mol wt 196.24. C 67.32%, H 8.22%, O 24.46%. Prepd by carboxylation of *d*-camphor: Brühl, *Ber.* 24, 3373 (1891).



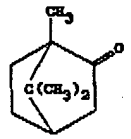
Crystals from benzene, water, ether, or 50% alcohol. mp 127-128°. Sparingly sol in cold water, more sol in warm water; sol in alcohol, ether, chloroform, in about 2 parts boiling benzene. Sparingly sol in cold benzene. Practically insol in cold petr ether; very slightly sol in boiling petr ether. For solu contg 0.38 g in 25 ml solvent: $[\alpha]_D$ +18° (benzene), +60° (alcohol), +73.3° (water).

Ammonium salt, $C_{11}H_{19}NO_3$, *camphyl*
phor solubilized.

Basic bismuth salt. $C_{22}H_{36}Bi_2O_{11}$. *Bi*
muth, Camphobismol. Prepn: Raiziss, C
1,921,638 (1933 to Abbott). Powder.
Practically insoluble in water; soluble i
benzene, oils.

THERAP CAT: Basic bismuth salt former

1710. Camphor. *1,7,7-Trimethylbicy*
one; 2-bornanone; 2-camphanone; 2-ke
norcamphane; gum camphor; Japan c
camphor; laurel camphor. $C_{10}H_{16}O$; n
78.89%, H 10.60%, O 10.51%. Occurs
camphor tree, *Cinnamomum camphora* I
er. *Lauraceae. Habit:* Java, Sumatra, C
inces), Japan, Formosa, Brazil. Obtainec
tion from comminuted trees which sho
years old. Description of various ind
Gubelmann, Elley, *Ind. Eng. Chem.* 26, 5
in Kirk-Othmer *Encyclopedia of Chemica*
(Wiley, New York, 2nd ed., 1964) pp 54
cesses start with vinyl chloride and cycl
tain the important intermediate dehydro
Review of syntheses: K. Alder in *New M*
tive Organic Chemistry (New York, 1948)
The Total Synthesis of Natural Products
Ed. (Wiley-Interscience, New York, 1
More than three-fourths of the camphor
produced synthetically (usually from pi
sold in the racemic form, although the
d-form. Config: Freudenberg *et al., A*



Translucent mass with crystalline frac
dral crystals from alcohol. Cubic cryst
chilling. Familiar fragrant and penetrati
bitter and cooling taste. d_4^{25} 0.992. mp 1
capillary, 2 mm diam). bp 204°. Sublir
room temp and press. *Keep in tight co*
heat. At 80° and 12 mm press 14% sublin
utes. Very volatile in steam. $[\alpha]_D^{25}$ +41° t
U.S.P. alcohol) according to U.S.P. speci
tent of the ethanol influences the rotation
+43.8° (c = 7.5 in abs alcohol). uv max
At 25° one gram dissolves in about 800
colloidal soln), in 1 ml alcohol, 1 ml eth
form, 0.4 ml benzene, 0.4 ml acetone, 1.
tine, 0.5 ml glacial acetic acid. Sol in ani
carbon disulfide, tetralin, decalin, methyl
in the higher alcohols, in fixed and volatil
conced mineral acids in phenol, in liquid
SO_2. Camphor has a peculiar tenacity a
dered in a mortar unless it is moistenec
solvent. Liquefies when triturated with
menthol, resorcinol, salol, *β*-naphthol,
urethan. LD_{50} i.p. in mice: 3000 mg/
Margolis, *Am. J. Pathol.* 30, 857 (1954).

Incompat: Incompatible with potassiu
salts of any kind should not be added t

Human Toxicity: Ingestion or injection
vomiting, vertigo, mental confusion, delir
sions, coma, respiratory failure, death. *Cl*
Commercial Products, R. E. Gosselin *et al.*
Wilkins, Baltimore, 4th ed., 1976) Secti

USE: Excellent plasticizer for cellulose
used in manuf of plastics, esp celluloid; in
nishes; in explosives; in pyrotechnics; as
embalming fluids; in manuf cymene; as pr
maceuticals and cosmetics.

THERAP CAT: Topical anti-infective; to